Short-term hypoxia improves early cardiac progenitor cell function in vitro.

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Authors: Ivan Hernandez, Jonathan M Baio, Eric Tsay, Aida F Martinez, Tania I Fuentes, Leonard L Bailey, Nahidh W Hasaniya, Mary Kearns-Jonker

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Public Summary:
The use of cardiovascular progenitor cells (CPCs) to repair damaged myocardium has been the focus of intense research. Previous reports have shown that pretreatments, including hypoxia, improve cell function. Our findings indicate that prior to transplantation, hypoxic preconditioning enhances CPC function, including invasion ability and pro-survival pathway activation.

Scientific Abstract:
The use of cardiovascular progenitor cells (CPCs) to repair damaged myocardium has been the focus of intense research. Previous reports have shown that pretreatments, including hypoxia, improve cell function. However, the age-dependent effects of short-term hypoxia on CPCs, and the role of signaling in these effects, are unknown. Cloned neonatal and adult CPCs expressing Isl1, c-Kit, KDR, PDGFRA, and CXCR4, were preconditioned using hypoxia (1% O2 for six hours). Intracellular signaling pathway changes were modeled using Ingenuity Pathway Analysis (IPA), while qRT-PCR, flow cytometry, and immunoblotting were used to measure pathway activation. Cellular function, including survival, cell cycle, and invasion, were evaluated using a TUNEL assay, flow cytometry, and a Transwell(R) invasion assay, respectively. IPA predicted, and RT-PCR and flow cytometry confirmed, that the PI3K/AKT pathway was activated following short-term hypoxia. Heat shock protein (HSP) 40 expression increased significantly in both age groups, while HSP70 expression increased only in neonatal CPCs. Neonatal CPC invasion and survival improved after hypoxia pre-treatment, while no effect was observed in cell cycling and developmental status. Prostaglandin receptor expression was enhanced in neonatal cells. Prior to transplantation, hypoxic preconditioning enhances CPC function, including invasion ability and pro-survival pathway activation.